REMARKS

Reconsideration and continuing examination of the above-identified application is respectfully requested in view of the amendments above and the discussion that follows.

Claims 1-23, 26-31, 36-37 and 43-50 were withdrawn due to their being directed to non-elected subject matter. Claims 11 and 36 were cancelled previously. Claims 24 and 25 have been amended pursuant to the Examiner's helpful suggestion. Claim 39 was amended to correct a spelling. Claims 24-25, 32-35 and 38-42 are in the case and are before the Examiner.

I. The Amendments

The specification has been amended pursuant to the Examiner's helpful suggestion for use of the headings. The text under the heading CROSS-REFERENCE TO RELATED APPLICATIONS provided citations to a German and PCT filing noted in the Application Data Sheet provided when the application was filed. An amended, shortened ABSTRACT is provided by the marked-up copy and an attached page at the end of this paper.

Claims 24 and 25 have been amended pursuant to the Examiner's helpful suggestion. No new matter has been added.

II. The Action

A. Rejection Under 35 USC §101

Claims 24 and 25 were rejected as allegedly not showing the "hand of man". The Action suggested corrective language, and although it cannot be agreed that the hand of man was not shown, the claims have been appropriately amended to speed prosecution.

B. First Rejection Under 35 USC §102

Claims 24 and 25 were rejected under 35 USC §102(b) as allegedly anticipated by the disclosures of Gebauer et al. (hereinafter Gebauer). The Action asserts that Gebauer teaches the isolation and separation of individual subunits from KLH2 and their molecular masses as assessed by SDS-PAGE, pointing specifically to Figure 4L of that paper that is said to show the isolation of the c subunit of KLH2 of *M. crenulata*. This basis for rejection cannot be agreed with and is respectfully traversed.

It is first noted that Gebauer does not teach the isolation of purified homogeneous subunits of KLH2, but only an analysis to determine the formerly unknown subunit organization of KLH2. Figure 4 to which the Action referred is an immunoelectrophoretic analysis of the KLH2 subunits and their fragments after limited proteolysis with a variety of enzymes. Although it is possible with this analytical method (in combination with HPLC and SDS) to identify the subunits of KLH2, it is not possible to obtain isolated protein as is presently claimed.

The fragments obtained by limited proteolysis always represent an mixture of different sequences. Even after anion exchange HPLC or SDS, there is always a 10%

molecular weight tolerance of the obtained "isolated" fragments using the Gebauer technique. The obtained fragments are sufficient to characterize the subunits of KLH2 and the sequencing of about 10 amino acid residues of each domain. However, the examples obtained by that method are not pure enough and not available in an amount sufficient to provide homogeneous, highly pure domains as can be achieved from the claimed subject matter of claims 24 and 25.

Thus, before this invention, one could not previously have been able to provide the isolated polypeptides of the claims. The impossibility of the isolation of a homogeneous polypeptide from a natural source and the complexity of the naturally occurring polypeptide prevents sequencing of KLH2 and each single domain thereof. The naturally occurring KLH2 is a very complex mixture of different oligomeric species comprising didecamers as well as polymeric microtube-like structures. Accordingly, nowhere in nature is a single isolatable protein of these claims. This basis for rejection should therefore be withdrawn.

C. Second Rejection Under 35 USC §102

Claims 38-42 were also rejected as allegedly anticipated, but here the anticipation was said to be by the disclosures of the 1995 Sigma Product Catalog, and particularly the teachings of a KLH composition from *M. crenulata* taught on page 520 that is understood to allegedly be a full length sequence. This basis for rejection cannot be agreed with and is respectfully traversed as discussed below.

It is respectfully submitted that there is no "full length" KLH in the form of a single molecule. Rather, KLH is a name for the mixture of the complex systems of KLH2 and KLH1 species in which each species comprises several oligomeric forms. As a result, pharmaceutical compositions as recited in claims 38-42 represent a homogeneous isolated protein that was never available in the art before the present invention was made. Every attempt in the prior art to provide a homogeneous isolated protein failed to produce a purified entity having to a single sequence with the minimal alternatives claimed. Those failures led to the present inventors determination of the subunit organization of KLH molecules and the resulting recombinant polypeptide. It is thus submitted that this basis for rejection should be withdrawn.

III. Further Argument

Because of the complex nature of the KLH mixtures that are available in nature, a skilled worker could not simply sequence the native protein -- there was none. In addition, in *M. crenulata,* there is no cDNA detectable that encodes KLH. Therefore, as noted at page 3 of the specification, cDNA could not be isolated from this animal. Accordingly, an alternative route was needed to obtain the claimed subject matter.

No primers or probes were known at the time the present invention was made. The alternative route that was successful here was to use probes designed from the closely related species *Haliotis tuberculata* that produces a similar haemocyanin subspecies that is designated Hth herein. It was only after designing cDNA primers and probes from Hth was the provision of cDNAs for KLH2

possible. This being the case, there was no reasonable expectation of success in making the claimed invention at the time it was made. As such, not only is the present invention not anticipated, it would also not have been obvious to a worker of ordinary skill at the time the invention was made.

IV. Information Disclosure Statement

The Action noted that European Patent Application EP 0 252 829 A1 was not considered because there was no English version or abstract provided. It has now been learned that EP 0 252 829 A1 has matured into US Patent No. 5,021,560. That US Patent is noted on the enclosed Form PTO-1449 and it is understood that being an issued US Patent, a physical copy is not required to be provided.

V. Summary

Claims 1-23, 26-31, 36-37 and 43-50 were withdrawn due to their being directed to non-elected subject matter and claims 11 and 36 were cancelled. Claims 24, 25 and 39 have been amended. Each basis for rejection or objection has been dealt with and overcome or otherwise made moot.

It is believed that this application is in condition for allowance of all of the pending claims. An early notice to that effect is earnestly solicited.

No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be the required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

Respectfully submitted,

By _____
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Enclosure
Petition and fee
Form PTO-1449
Abstract page

CERTIFICATE OF MAILING

I hereby certify that this Reply and Amendment, Form PTO-1449, along with a Petition for an Extension of Time and its fee are being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on September 19, 2005.

By _____
Edward P. Gamson